
Specific Targeting Hypoxia Metastatic Breast Tumor with Allogeneic Off-the-Shelf Anti-EGFR CAR NK Cells Expressing an ODD domain of HIF-1 α

Grant Award Details

Specific Targeting Hypoxia Metastatic Breast Tumor with Allogeneic Off-the-Shelf Anti-EGFR CAR NK Cells Expressing an ODD domain of HIF-1 α

Grant Type: Therapeutic Translational Research Projects

Grant Number: TRAN1-14003

Investigator:

Name:	Jianhua Yu
Institution:	City of Hope, Beckman Research Institute
Type:	PI

Award Value: \$6,036,002

Status: Pre-Active

Grant Application Details

Application Title: Specific Targeting Hypoxia Metastatic Breast Tumor with Allogeneic Off-the-Shelf Anti-EGFR CAR NK Cells Expressing an ODD domain of HIF-1 α

Public Abstract:**Translational Candidate**

EGFR-CAR_sIL15 NK cells derived from CD34(+) umbilical cord blood hematopoietic stem cells

Area of Impact

patients with metastatic breast cancer, especially HER2-low breast cancer

Mechanism of Action

EGFR-CAR_sIL15 NK cells are umbilical cord blood-derived CD34+ HSCs that are engineered to target EGFR and express soluble IL-15, and then are differentiated into NK cells. To reduce potential off-target toxicity, our CAR is fused with the oxygen-dependent degradation domain (ODD) of HIF1a, leading to functionality in the tumor microenvironment with low oxygen levels, while CAR will not express or have a limited expression level in the normal tissues with relatively high levels of oxygen.

Unmet Medical Need

Breast cancer (BC) is the most common cancer and second leading cause of cancer death in women in North America. Successful translation of our safe, "off-the-shelf" cellular therapy of EGFR-CAR_sIL15 NK cells will diminish the life-threatening clinical manifestations of metastatic BC patients.

Project Objective

Complete Pre-IND submission and finalize IND plans

Major Proposed Activities

- Manufacture EGFR-CAR_sIL15 NK cells and PK/PD study
- Pharmacology toxicity and optimize treatment schedule of EGFR-CAR_sIL15 NK cells in efficacy testing
- Confirm efficacy of EGFR-CAR_sIL15 NK cells under optimized and safe conditions and Pre-IND submission

Statement of Benefit to California:

In the United States, currently, breast cancer (BC) is the most common cancer, and it is the second leading cause of cancer death, including in California. While there has been a decline in BC deaths over the last 30 years, there is a persistent mortality gap between Black women and white women. Our goal is to develop an "off-the-shelf," ready-to-use cell therapy that is appropriate and easily accessible for any patient regardless of race, ethnicity, age, or socioeconomic status.

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